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(54) MATERIAL AND MODULE FOR HEMOCATHARSIS USING THE SAME

(57)Abstract:

PROBLEM TO BE SOLVED: To provide a material which can suppress activation of blood platelets while retaining an insolubilized condition of a polyvinyl pyrrolidone and its production method.

SOLUTION: The material comprises forming a separation membrane composed of polyvinyl pyrrolidone having a variable amount of ≥ 300 and a soluble amount of ≤ 15 wt.%.

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CLAIMS

[Claim(s)]

[Claim 1] The ingredient characterized by being an ingredient containing a polyvinyl pyrrolidone, and for the mobile amount of this polyvinyl pyrrolidone being 300 or more, and the amount of fusibility being 15 or less % of the weight.

[Claim 2] The ingredient according to claim 1 with which an ingredient is characterized by this base material being a polysulfone system polymer including a polyvinyl pyrrolidone and its base material.

[Claim 3] The ingredient according to claim 1 or 2 characterized by the gestalt of an ingredient being a demarcation membrane.

[Claim 4] The ingredient according to claim 1 to 3 characterized by the gestalt of an ingredient being a hollow fiber.

[Claim 5] The ingredient according to claim 3 or 4 characterized by a demarcation membrane being an object for blood purification.

[Claim 6] The module for blood purification characterized by coming to build a demarcation membrane according to claim 1 to 5.

[Claim 7] The module for blood purification according to claim 6 characterized by using as an artificial kidney.

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention is used about an ingredient suitable for the polysulfone system demarcation membrane which has especially anti-platelet adhesion.

[0002]

[Description of the Prior Art] Although current and various polymeric materials are used in the medical field, in the tools with which direct blood, such as an artificial blood vessel, a catheter, a blood bag, and an artificial kidney, contacts, adhesion of constituents of blood, such as a plasma protein and a platelet, and formation of the thrombus resulting from this are big problems. In the demarcation membrane used especially for blood purification, activation of a platelet may cause residual blood. Therefore, in order to solve these problems, a blood compatible material with little platelet adhesion is desired.

[0003] Conventionally, as a material of the charge of blood purification material, high molecular compounds, such as a cellulose, cellulose acetate, cellulose triacetate, polyolefine, polyimide, a polycarbonate, polyarylate, polyester, a polyacrylonitrile, a polymethyl methacrylate, a polyamide, and a polysulfone system polymer, have been used. Also in it, the polysulfone system polymer is excellent in thermal resistance, and is used for various demarcation membranes, films, etc. including permeable membrane. Especially when used as a charge of blood purification material, in order to give haemocompatibility, hydrophilic giant molecules, such as a polyvinyl pyrrolidone, are blended and it is used.

[0004] In order to prevent the elution from the film, insolubilization processing of the polyvinyl pyrrolidone blended by the demarcation membrane is usually carried out by radiation irradiation etc. However, if insolubilization processing is carried out, when blood contacts a film front face, a platelet is activated, and it is known that residual blood will increase in number (reference, such as the patent reference 1).

[0005]

[Patent reference 1] JP,9-323031,A [0006]

[Problem(s) to be Solved by the Invention] The purpose of this invention is to offer the ingredient which controls activation of a platelet, and the blood compatible material using it, improved the fault of this conventional technique and insolubilized a polyvinyl pyrrolidone especially.

[0007]

[Means for Solving the Problem] In order to solve the above-mentioned technical problem, this invention has the following configurations.

[0008] That is, this invention is an ingredient which consists of a polyvinyl pyrrolidone, and is an ingredient characterized by for the mobile amount of this polyvinyl pyrrolidone being 300 or more, and the amount of fusibility being 15 or less % of the weight.

[0009] Moreover, this invention relates to the module having this ingredient.

[0010] Furthermore, the manufacture approach of the ingredient of this invention is insoluble or the manufacture approach of an ingredient characterized by using the system which added the additive made to swell as a film production undiluted solution about this polysulfone system

polymer at the solution which carried out the mixing dissolution of the polyvinyl pyrrolidone with the solvent at the polysulfone system polymer.

[0011]

[Embodiment of the Invention] As a polyvinyl pyrrolidone used by this invention, although especially the weight average molecular weight is not limited, 2000-2 million are desirable and 10000-1500000 are more desirable. From the point of the ease of acquisition, the weight average molecular weight 1,100,000 marketed, 45,000, 29,000, and the thing of 9000 and 2900 are used suitably. In addition, the weight average molecular weight of the polyvinyl pyrrolidone described here is the molecular weight in the raw material phase used for an ingredient. In the produced ingredient, when means, such as radiation bridge formation, are used, the molecular weight of a polyvinyl pyrrolidone is bigger than the molecular weight in a raw material phase.

[0012] As an example of goods of a polyvinyl pyrrolidone, "Kollidon" 12 PF, this 17 PF -- said -- 25 -- said -- 30 -- said -- 90 (BASF A.G. make) and a "ruby squall" -- K 17 -- said -- K 30 -- said -- K 80 -- said -- K 90 (BASF A.G. make) -- a "plus boss" -- K-29 / 32 -- said -- K-25 -- said -- polyvinyl pyrrolidones, such as K-90, this K-90D, and this K90-M (ISP company make), are mentioned.

[0013] Although a homopolymer is suitable for the polyvinyl pyrrolidone used by this invention, copolymerization of it may be carried out to other monomers in the range which does not bar the effectiveness of this invention. Here, although especially the amount of other copolymerization monomers is not limited, it is desirable that it is 80 or less % of the weight.

[0014] As an example of goods of a polyvinyl-pyrrolidone copolymer "Kollidon" VA 64, (squall by BASF A.G.) VA 64 (BASF A.G. make), ["ruby squall"] "ruby tech" VPI55 K18P -- said -- VPI55 K72W -- said -- Quat 73W -- said -- VPMA 91W -- said -- VPC 55 K65W (BASF A.G. make) and a "plus boss" -- polyvinyl-pyrrolidone copolymers, such as S-630 (ISP company make), are mentioned.

[0015] Although the ingredient of this invention contains a polyvinyl pyrrolidone, it is desirable to hold a polyvinyl pyrrolidone to stability as an ingredient gestalt, to compound the material which serves as a base material of a polyvinyl pyrrolidone in order to prevent being eluted in large quantities, deforming, or collapsing, and to use. Although the laminating of the material and polyvinyl pyrrolidone which especially the configuration / compound approach with the material used as a polyvinyl pyrrolidone and said base material is not limited, and serve as a base material may be carried out, to be mixed or dissolved is more desirable.

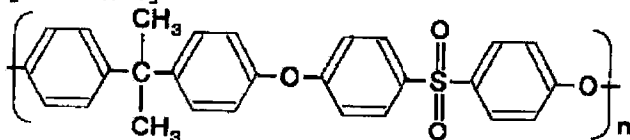
[0016] Moreover, although not limited especially as a material used as a base material, it is desirable that it is an organic macromolecule polymer. As this organic macromolecule polymer, a polysulfone system polymer is used preferably.

[0017] Although especially the amount of the polyvinyl pyrrolidone contained in the ingredient of this invention is not limited, when it is many, since a certain amount of reinforcement is required for a base material, it is preferably desirable [an amount] that it is [1 % of the weight or more] 10 or less % of the weight 50 or less % of the weight 0.1 % of the weight or more still more preferably. this content is independent in well-known approaches, such as elemental analysis and NMR (nuclear magnetic resonance analysis), -- or it can combine and check.

[0018] The polysulfone system polymer preferably used as a material of an ingredient by this invention has a ring, a sulfonyl radical, and a ether group in a principal chain, and although the polysulfone shown with the following chemical formula 1 and a chemical formula 2 is used suitably, it is not limited to these by this invention. Here, n in a formula is an integer which shows polymerization degree, and is the integer of the range of 50-80 preferably.

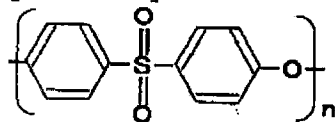
[0019]

[Formula 1]



[0020]

[Formula 2]



[0021] as the example of goods of polysulfone — "YUDERU" — P-1700 — said — P-3500 (product made from TEIJINAMOKO) — an "ultra zone" — S3010 — said — S6010 (BASF A.G. make) and "Vitrex" (Sumitomo Chemical) — "Leh Dell" A-200A — said — A-300 and "Leh Dell" — R-5000 — said — R-5800 (product made from TEIJINAMOKO), and an "ultra zone" — polysulfones, such as E (BASF A.G. make) and "SUMIKA Excel" (Sumitomo Chemical Co., Ltd. make), are mentioned.

[0022] Although the polymer which consists only of a repeat unit expressed with the above-mentioned chemical formula 1 and/or the above-mentioned chemical formula 2 is suitable for the polysulfone used by this invention, it may copolymerize with other monomers in the range which does not bar the effectiveness of this invention. Although especially the addition of other copolymerization monomers is not limited, it is desirable that it is 10 or less % of the weight.

[0023] Polymers, additives, etc. other than the material used as said polyvinyl pyrrolidone and base material may be mixed by the ingredient of this invention in the range which does not bar the effectiveness of this invention. Although especially additions other than the material used as a polyvinyl pyrrolidone and a base material are not necessarily limited, it is desirable that it is 10 or less % of the weight.

[0024] that to which especially the gestalt of the ingredient of this invention is limited — it is not — for example, the shape of a tube and a bead — it knits and is used with gestalten, such as a ground, a nonwoven fabric, a cut fiber, a flat film, and a hollow fiber. Moreover, what cast the ingredient in the specific form dissolved in the solvent, and the coated thing may be used. However, if it is the case where it uses for processing effectiveness, i.e., a blood processing application, etc., when the reservation of surface area in contact with blood etc. will be taken into consideration, it is desirable that it is a hollow fiber.

[0025] Moreover, as for the ingredient of this invention, being used as a demarcation membrane is desirable. The thickness in that case has desirable 10–80 micrometers, and its 20–50 micrometers are more desirable. Moreover, about a membranous average aperture, it is desirable that 1% albumin permeability is 0.5% or more, and 1% or more is more desirable. In the case of a hollow fiber, as for the bore of a hollow filament, it is desirable that it is 100–300 micrometers, and its 150–200 micrometers are more desirable.

[0026] When considering as the gestalt of a hollow fiber, the approach learned conventionally can be used as the manufacture approach of the hollow fiber. There are the following approaches as a desirable approach in the case of using polysulfone with a polyvinyl pyrrolidone.

[0027] That is, they are insoluble or the manufacture approach of a demarcation membrane characterized by using the system which added the additive made to swell as a film production undiluted solution about this polysulfone system polymer at the solution which carried out the mixing dissolution of a polysulfone system polymer and the polyvinyl pyrrolidone with the solvent.

[0028] Here, as for the weight ratio of a polysulfone system polymer and a polyvinyl pyrrolidone, 20:1–1:5 are desirable, and 5:1–1:1 are more desirable.

[0029] Moreover, as a good solvent for carrying out the mixing dissolution of a polysulfone system polymer and the polyvinyl pyrrolidone, N,N-dimethylacetamide, dimethyl sulfoxide, dimethylformamide, N-methyl pyrrolidone, dioxane, etc. are used preferably. The concentration of a polysulfone system polymer has 10 – 30 desirable % of the weight, and its 15 – 25 % of the weight is more desirable.

[0030] Although there are water, a methanol, ethanol, isopropanol, a hexanol, 1,4-butanediol, etc. considering a polysulfone system polymer as insoluble or an additive made to swell, for example, considering a production cost, water is used especially preferably. When water is used,

since the freezing characteristic of a polysulfone system polymer is high, especially the addition of water has 1 - 5 % of the weight desirable [here,] 7 or less % of the weight. When using an additive with small freezing characteristic, an addition may increase, and a suitable amount can be chosen suitably.

[0031] Especially the approach of producing a film using said film production undiluted solution is not limited, but can use a well-known approach, for example, a duplex -- annular -- in case the regurgitation of the film production undiluted solution is carried out from a mouthpiece, the approach of leading infusion to a coagulation bath after making it running a sink and the dry type section can be used inside. Under the present circumstances, since the humidity of the dry type section affects it, it is also possible to speed up the phase separation behavior near the outside surface, to expand an aperture, and to reduce the transparency and diffused resistor in the case of dialysis as a result by the hydration from a film outside surface, during dry type section transit. However, when relative humidity is too high, the undiluted solution coagulation in an outside surface becomes dominant, an aperture becomes small on the contrary, and there is an inclination which increases transparency and diffused resistor of a demarcation membrane as a result. Therefore, as relative humidity of the dry type section, 60 - 90% is suitable. Moreover, it is desirable to use what consists of a presentation based on the solvent used for the film production undiluted solution from process fitness as a presentation of infusion. Here, as concentration of infusion, when dimethylacetamide is used, for example, 45 - 80 % of the weight is desirable, and 60 - 75% of the weight of a water solution is used suitably more preferably.

[0032] Moreover, in this invention, although the polyvinyl pyrrolidone in an ingredient is insolubilized, it is desirable to carry out bridge formation processing of the polyvinyl pyrrolidone contained in an ingredient, using a radiation as an approach of insolubilizing.

[0033] As radiation treatment, it is desirable to irradiate an ingredient to a damp or wet condition gamma ray, an electron ray, etc. A damp or wet condition here means the thing in the condition of not drying an ingredient. Although especially the extent is not limited, it is usually desirable that the ingredient contains 1% of the weight or more of moisture to the weight of an ingredient. Moreover, in the condition of having been immersed in the water solution is sufficient as an ingredient.

[0034] The absorbed dose of a radiation has desirable 10 - 50kGy extent at a damp or wet condition, and when the dosage exceeding 20kGy is irradiated, it is also possible to perform sterilization processing to coincidence. Under the present circumstances, a dosimetry label can be stuck on the surface of a module, and an absorbed dose can measure it.

[0035] The ingredient by which radiation treatment was carried out can be suitably used as a demarcation membrane for blood purification. When using for blood purification, the sterilization effectiveness will also do radiation treatment so to coincidence, but if wet sterilization etc. is performed after carrying out radiation irradiation and insolubilizing a polyvinyl pyrrolidone when the sterilization effectiveness runs short, it is suitably usable as a charge of blood purification material.

[0036] In less than 10 kGies, it is hard to insolubilize a polyvinyl pyrrolidone for the absorbed dose of a radiation. Moreover, when an exposure increases more than 50kGy, the effect of degradation for other materials, such as polysulfone which is a base material, and a case, may become large.

[0037] In order to raise the mobile amount of a polyvinyl pyrrolidone, insolubilized a polyvinyl pyrrolidone, it can obtain by performing radiation treatment, where humidity of the ingredient containing a polyvinyl pyrrolidone is carried out to the water solution containing a bridge formation inhibitor.

[0038] As this bridge formation inhibitor, especially if crosslinking reaction is checked, it is not limited, but since it is necessary to take the safety into consideration in case it uses for a blood purification application, a toxic low thing is used suitably. Especially, the mineral salt of saccharides, such as alcohols, such as water soluble vitamin, a glycerol, and ethanol, polyphenol, polyethyleneimine, a polyethylene glycol, and trehalose, a sodium pyrosulfite, a sodium hydrogencarbonate, etc., oxygen, a carbon dioxide, etc. are mentioned, and it is used suitably.

These bridge formation inhibitors may be used independently, and two or more kinds may be mixed and they may be used.

[0039] Although the suitable range changes with bridge formation inhibitors to contain, even when using which bridge formation inhibitor, it is necessary to make the mobile amount of a polyvinyl pyrrolidone or more into 300, and to make the amount of fusibility below into 15% weight about the concentration of the water solution containing a bridge formation inhibitor. For example, although it is suitable that glycerol concentration is [in the case of a glycerol water solution] 0.01 % of the weight or more and 5 % of the weight or less in the case of 0.1 % of the weight or more, 10 % of the weight or less, and an ethanol water solution, as for the case of 0.01 % of the weight or more, 5 % of the weight or less, and a polyethyleneimine water solution, in the case of other bridge formation inhibitors, a suitable density range can be chosen, respectively.

[0040] Moreover, in order to carry out fusibility to 15 or less % of the weight, it is considered that are desirable and it is moderately desirable that a polyvinyl pyrrolidone is in the condition which contacted and became entangled to keep moderate the distributed condition of the polyvinyl pyrrolidone before irradiating not only selection of a bridge formation inhibitor but a radiation. Although what is necessary is just to choose the presentation of an ingredient, a mixed approach, and the molding approach as an approach so that fusibility may become 15 or less % of the weight, it is a desirable approach to make high the polyvinyl-pyrrolidone content in a membrane formation undiluted solution, and it can make fusibility low, for example, bridge formation progressing and maintaining a mobile amount highly, when fusibility was high and the polyvinyl-pyrrolidone content was made high. When the polyvinyl-pyrrolidone content in a flat film was 1 % of the weight in the polysulfone / polyvinyl-pyrrolidone flat film which it evaporated [flat film] and dried dimethylacetamide after dissolving polysulfone and PVP in dimethylacetamide enough, if an example is given, all had dissolved after radiation irradiation, but when the content of a polyvinyl pyrrolidone was 66 % of the weight, even if it was the same membrane formation and radiation treatment conditions except the presentation, fusibility was 15 or less % of the weight. If an example is given in the case of a hollow fiber, using the membrane formation solution with which 8 % of the weight or more of polyvinyl pyrrolidones with larger weight average molecular weight than 45,000, 18 % of the weight of polysulfones, 1 % of the weight of water, and the remainder consist of dimethylacetamide, a hollow fiber will be created and it will be obtained by carrying out gamma irradiation in the water solution containing 0.1 % of the weight - 10 % of the weight of glycerol concentration. Moreover, if conditions, such as making [many] the content of a polyvinyl pyrrolidone, are suitably chosen when the fusibility which in other cases makes [many] the amount of bridge formation inhibition material when the movability is low is high, the ingredient used as the purpose can be obtained.

[0041] The amount of fusibility of a polyvinyl pyrrolidone here is carried out as follows, and is calculated. That is, the dry ingredient is dissolved in a N-methyl-2-pyrrolidone at 2.5% of the weight of concentration, amount addition of the water is carried out 1.7 times at the solution, and a material polymer is deposited. The polyvinyl pyrrolidone of fusibility is contained in a solution with the dispersed polysulfone particle. the nonaqueous filter (the TOSOH make, diameter of 2.5micro) for HPLC (high performance chromatography) filters and removes the polysulfone particle in a solution, and the quantum of the polyvinyl pyrrolidone contained in a filtrate is carried out in HPLC (equipment: -- Waters, GPC-244, two column:TSKgelGMPWXL(s), solvent:****, a 0.1M ammonium chloride, 0.1-N ammonia, pH 9.5, rate-of-flow:1.0 ml/min, and temperature:23 degree C). The value broken by the amount of all the polyvinyl pyrrolidones contained in per [which is asked for the amount of fusibility of the polyvinyl pyrrolidone contained in per unit weight of an ingredient from the amount of the polyvinyl pyrrolidone contained in a filtrate, and is asked for it from ultimate analysis] unit weight of an ingredient is the amount of fusibility (%).

[0042] Furthermore, the mobile amount of a polyvinyl pyrrolidone here is carried out as follows, and is calculated.

[0043] That is, NMR (nuclear magnetic resonance analysis) using a high-resolution MAS (Magic Angle Spinning, Magic include-angle rotation method) solution probe is used. It is immersed in

heavy water of an overlarge, and, specifically, the heavy water permutation of the demarcation membrane of the damp or wet condition washed with distilled water is carried out. This actuation also removes additives, such as a bridge formation inhibitor, as much as possible to coincidence. Next, it puts carrying out humidity of the sample (the sample weight when drying is 5mg) permuted with heavy water to an exclusive cel with a capacity [l] of 40micro, and the UNITY INOVA600 mold equipment made from VARIAN performs 1 H-NMR measurement (sufficiently long repetition time is set up.). It is TSP:3-trimethylsilyl sodium propionate as an inner label. - 2, 2, 3, and 3-d4 Let about 10micro g addition of heavy water solutions, and a HDO peak be elimination and the MAS rotational frequency of 1600-1800Hz by pre-SACHURESHON. In the obtained spectrum, when the integral value of the peak (-0.2-0.2 ppm) of TSP is set to 1000.00, it asks for the peak area of the polyvinyl-pyrrolidone origin located in 2.9-4.2 ppm. When blocked at the peak which originates in a bridge formation inhibitor (for example, polyethyleneimine) near the, it can ask for the peak area of the polyvinyl-pyrrolidone origin located in 1.4-2.6 ppm, and can ask for the real area of the peak of the polyvinyl-pyrrolidone origin located in 2.9-4.2 ppm from the calibration curve created from the peak area with various movability of 1.4-2.6 ppm and 2.9-4.2 ppm of a sample. This peak area is equivalent to the amount of the polyvinyl pyrrolidone contained in an ingredient. Then, the mobile amount of a polyvinyl pyrrolidone means the thing of all the polyvinyl pyrrolidones in the ingredient asked for the peak area called for as mentioned above from ultimate analysis comparatively broken by (%).

[0044] In addition, the total amount of polyvinyl pyrrolidones in an ingredient can be calculated by elemental analysis. That is, the nitrogen monoxide which 0.2-0.5mg of dry ingredients was evaporated and oxidized, and generated them with the horizontal-type fission reactor (800-950 degrees C) is measured with a chemiluminescence method (equipment Mitsubishi Chemical TN-10 use). A quantum can carry out concentration count automatically beforehand by the calibration curve created by the standard of a nitrogen-containing polymer.

[0045] Hereafter, the platelet adhesion experiment approach in case the ingredient of this invention is a hollow fiber is indicated.

[0046] Both ends are fixed to a glass tube module case by the epoxy system potting agent so that a hollow filament centrum may not be blockaded for a hollow filament demarcation membrane in 30 bundles, and a mini module is created. The diameter of this mini module is about 7mm, and die length is about 10cm. After a silicone tube's tying the blood inlet port and dialysing fluid outlet of this mini module and washing a sink, a hollow filament, and the interior of a module for 100ml of distilled water from a blood outlet by the 10ml rate of flow for /, it is filled up with a physiological saline and a dialysing fluid inlet port and an outlet are capped. Next, after carrying out the physiological saline priming of the hollow filament side for 2 hours by the 0.59ml rate of flow for /, it flows in for 1 hour by the 0.59ml rate of flow for /in 7ml of blood which mixed rabbit fresh blood with the citric-acid 3 sodium 2 hydrate water solution by 1:9 (volume ratio) 3.2%. Then, a physiological saline washes in 10ml syringe, a hollow filament and dialysing fluid side is filled up with a glutaraldehyde water solution 3%, and more than every night and glutaraldehyde immobilization are performed. Then, with distilled water, glutaraldehyde was washed, and from the mini module, the hollow fiber was started and it dried. The internal surface of this hollow fiber was observed with the scanning electron microscope, and 1.12x10³ micrometers of adhesion platelet counts in the area of 2 were counted. An adhesion platelet count is the demarcation membrane excellent in little direction. What is necessary is to immerse an ingredient in blood, when it is not the gestalt of a hollow fiber, to observe an adhesion condition, or to install a plate in the bottom of cylinder tubing in the case of a monotonous gestalt, to put in blood, and just to carry out suitably.

[0047] The ingredient in this invention can be suitably used as charges of blood purification material, such as transparence resin, a medical-application hydro gel ingredient of a contact lens intraocular implant and others, hemodialysis film, and an artificial kidney.

[0048]

[Example] In the NMR measurement in an example, the demarcation membrane carried out

refrigeration immersion for 12 hours at membranous heavy water of 1000 time weight. 45-degree pulse performed measurement in repetition-time 10 seconds.

[0049] (Example 1) The polysulfone (product made from TEIJINAMOKO "YUDERU" P- 3500) 18 section and the polyvinyl-pyrrolidone (BASF A.G. make "Kollidon" 30) 9 section were added to the N,N-dimethylacetamide 72 section and the water 1 section, and the heating dissolution was carried out for 90-degree-C 14 hours. this film production undiluted solution -- orifice mold duplex cylindrical with an outer diameter [of 0.3mm], and a bore of 0.2mm -- after making the solution which consists of the dimethylacetamide 58 section and the water 42 section as discharge core liquid breathe out and passing 350mm of dry type length from a mouthpiece, it led to the coagulation bath of 100% of water, and the hollow fiber was obtained. The paths of the obtained hollow filament were the bore of 200 micrometers, and 40 micrometers of thickness. Gamma irradiation of the obtained hollow fiber was carried out in the water solution containing 1 % of the weight of glycerols. Gamma ray absorbed doses were 28kG(ies). The mobile amount of the polyvinyl pyrrolidone in this hollow fiber, the amount of fusibility, and the number of platelet adhesion were shown in Table 1.

[0050] (Example 2) Gamma irradiation of the hollow fiber obtained like the example 1 was carried out in the water solution containing 0.5 % of the weight of glycerols. Gamma ray absorbed doses were 29kG(ies). The mobile amount of the polyvinyl pyrrolidone in this hollow fiber, the amount of fusibility, and the number of platelet adhesion were shown in Table 1.

[0051] (Example 3) Gamma irradiation of the hollow fiber obtained like the example 1 was carried out in the water solution containing 0.1 % of the weight of glycerols. Gamma ray absorbed doses were 29kG(ies). The mobile amount of the polyvinyl pyrrolidone in this hollow fiber, the amount of fusibility, and the number of platelet adhesion were shown in Table 1.

[0052] (Example 4) Gamma irradiation of the hollow fiber obtained like the example 1 was carried out in the water solution containing 1 % of the weight (Wako Pure Chem, molecular weight 70,000) of polyethyleneimine. Gamma ray absorbed doses were 29kG(ies). The mobile amount of the polyvinyl pyrrolidone in this hollow fiber, the amount of fusibility, and the number of platelet adhesion were shown in Table 1. In addition, about the mobile amount, since the peak of the polyvinyl-pyrrolidone origin located in 2.9-4.2 ppm was blocked at the peak originating in polyethyleneimine, it asked for the peak area of the polyvinyl-pyrrolidone origin located in 1.4-2.6 ppm, and asked for the area of the peak of the polyvinyl-pyrrolidone origin located in 2.9-4.2 ppm from the calibration curve created from the peak area of 1.4-2.6 ppm and 2.9-4.2 ppm.

[0053] (Example 1 of a comparison) Gamma irradiation of the hollow fiber obtained like the example 1 was carried out underwater. Gamma ray absorbed doses were 29kG(ies). The mobile amount of the polyvinyl pyrrolidone in this hollow fiber, the amount of fusibility, and the number of platelet adhesion were shown in Table 1.

[0054] (Example 2 of a comparison) Gamma irradiation was carried out where humidity of the hollow fiber obtained like the example 1 is carried out in the water solution containing 80 % of the weight of glycerols. Gamma ray absorbed doses were 29kG(ies). The mobile amount of the polyvinyl pyrrolidone in this hollow fiber, the amount of fusibility, and the number of platelet adhesion were shown in Table 1.

[0055] (Example 3 of a comparison) commercial Asahi medical company make -- the hollow filament was taken out from "APS-150S" (thing [finishing / lot number 008L8 V-S and gamma ray sterility]). The mobile amount of the polyvinyl pyrrolidone in this hollow fiber, the amount of fusibility, and the number of platelet adhesion were shown in Table 1.

[0056] (Example 4 of a comparison) The hollow filament was taken out from commercial "PS-UW" made from the Kawasumi chemistry (thing [finishing / a lot number 082675 and autoclave sterilization]). The mobile amount of the polyvinyl pyrrolidone in this hollow fiber, the amount of fusibility, and the number of platelet adhesion were shown in Table 1.

[0057] (Example 5 of a comparison) Gamma irradiation was carried out like the example 1 in the water solution containing 0.05 % of the weight of glycerols. Gamma ray absorbed doses were 27kG(ies). The mobile amount of the polyvinyl pyrrolidone in this hollow fiber, the amount of fusibility, and the number of platelet adhesion were shown in Table 1.

[0058]

[Table 1]

	可動性量	可溶性量(重量%)	血小板付着数
実施例1	911	10.3	18
実施例2	1159	8.3	17
実施例3	716	7.7	20
実施例4	1940	12.2	9
比較例1	147	3.5	47
比較例2	1220	73.3	5.7
比較例3	1036	19.5	0
比較例4	1263	46.3	0
比較例5	280	5.1	29

[0059] Each demarcation membrane of Table 1 to an example was an outstanding demarcation membrane with few platelet adhesion. On the other hand, the example of a comparison with the mobile small amount of a polyvinyl pyrrolidone (examples 1 and 5 of a comparison) had many platelet adhesion. Moreover, although the example of a comparison (examples 2, 3, and 4 of a comparison) which is too large has few platelet adhesion, we are anxious about the elution of the polyvinyl pyrrolidone of fusibility.

[0060]

[Effect of the Invention] The ingredient and its manufacture approach of this invention are used for the application of blood purifier etc., can offer the ingredient excellent in especially anti-platelet adhesion, and are very useful.

[Translation done.]

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(54)【発明の名称】 材料およびそれを用いた血液浄化用モジュール

(57)【要約】

【課題】ポリビニルピロリドンを不溶化したままで、血小板の活性化を抑制する材料およびその製造方法を提供すること。

【解決手段】ポリビニルピロリドンからなる分離膜であって、該ポリビニルピロリドンの可動性量が300以上、かつ、可溶性量が15重量%以下であることを特徴とする材料。

【特許請求の範囲】

【請求項1】 ポリビニルピロリドンを含む材料であって、該ポリビニルピロリドンの可動性量が300以上、かつ、可溶性量が15重量%以下であることを特徴とする材料。

【請求項2】 材料がポリビニルピロリドンとその支持体とを含み、該支持体がポリスルホン系ポリマーであることを特徴とする請求項1に記載の材料。

【請求項3】 材料の形態が分離膜であることを特徴とする請求項1または2に記載の材料。

【請求項4】 材料の形態が中空糸膜であることを特徴とする請求項1～3のいずれかに記載の材料。

【請求項5】 分離膜が血液浄化用であることを特徴とする請求項3または4に記載の材料。

【請求項6】 請求項1～5のいずれかに記載の分離膜を内蔵してなることを特徴とする血液浄化用モジュール。

【請求項7】 人工腎臓として用いることを特徴とする請求項6記載の血液浄化用モジュール。

【発明の詳細な説明】

【0001】

【発明の属する技術分野】本発明は、材料に関するものであり、特に抗血小板付着性を有するポリスルホン系分離膜に好適に用いられる。

【0002】

【従来の技術】現在、様々な高分子材料が医療分野で使用されているが、人工血管、カテーテル、血液バッグ、人工腎臓などの直接血液の接触する用具においては血漿蛋白や血小板などの血液成分の付着、およびこれに起因する血栓の形成は大きな問題である。特に血液浄化に使用される分離膜では、血小板の活性化は残血を引き起こす可能性がある。したがって、これらの問題を改善するために、血小板付着の少ない血液適合性材料が望まれている。

【0003】従来、血液浄化用材料の素材としては、セルロース、セルロースアセテート、セルローストリアセテート、ポリオレフィン、ポリイミド、ポリカーボネート、ポリアリレート、ポリエステル、ポリアクリロニトリル、ポリメタクリル酸メチル、ポリアミド、ポリスルホン系ポリマーなどの高分子化合物が用いられてきた。その中でもポリスルホン系ポリマーは耐熱性に優れており、透析膜をはじめとして種々の分離膜やフィルムなどに用いられている。特に血液浄化用材料として使用されるときは、血液適合性を付与するためにポリビニルピロリドンなどの親水性高分子をブレンドして用いられている。

【0004】分離膜にブレンドされているポリビニルピロリドンは、膜からの溶出を防ぐために、通常、放射線照射などにより、不溶化処理されている。しかし、不溶

性化し、残血が増えることが知られている（特許文献1など参照）。

【0005】

【特許文献1】特開平9-323031号公報

【0006】

【発明が解決しようとする課題】本発明の目的は、かかる従来技術の欠点を改良し、特に、ポリビニルピロリドンを不溶化したままで、血小板の活性化を抑制する材料およびそれを用いた血液適合性材料を提供することにある。

【0007】

【課題を解決するための手段】上記課題を解決するため、本発明は以下の構成を有する。

【0008】すなわち本発明は、ポリビニルピロリドンからなる材料であって、該ポリビニルピロリドンの可動性量が300以上、かつ、可溶性量が15重量%以下であることを特徴とする材料である。

【0009】また、本発明は、この材料を内蔵したモジュールに関する。

【0010】さらに、本発明の材料の製造方法は、ポリスルホン系ポリマーに、ポリビニルピロリドンを溶媒で混和溶解した溶液に、該ポリスルホン系ポリマーを不溶または膨潤させる添加剤を加えた系を製膜原液として用いることを特徴とする材料の製造方法である。

【0011】

【発明の実施の形態】本発明で用いられるポリビニルピロリドンとしては、その重量平均分子量は特に限定されるものではないが、2000～2000000が好ましく、10000～1500000がより好ましい。入手の容易さの点からは、市販されている重量平均分子量110万、4.5万、2.9万、9000、2900のもの好適に用いられる。なお、ここで記したポリビニルピロリドンの重量平均分子量は、材料に使用する原料段階での分子量である。作製された材料において、放射線架橋などの手段を用いた場合にはポリビニルピロリドンの分子量は、原料段階での分子量より大きなものとなっている。

【0012】ポリビニルピロリドンの商品例としては、“コリドン”12PF、同17PF、同25、同30、同90（BASF社製）、“ルビスコール”K17、同K30、同K80、同K90（BASF社製）、“プラスドン”K-29/32、同K-25、同K-90、同K-90D、同K90-M（ISP社製）等のポリビニルピロリドンが挙げられる。

【0013】本発明で用いられるポリビニルピロリドンは、ホモポリマーが好適であるが、本発明の効果を妨げない範囲で他のモノマーと共重合されたものであってもかまわない。ここで、他の共重合モノマーの量は特に限定するものではないが、80重量%以下であることが好

【0028】ここで、ポリスルホン系ポリマーとポリビニルピロリドンの重量比率は、20：1～1：5が好ましく、5：1～1：1がより好ましい。

【0029】また、ポリスルホン系ポリマーとポリビニルピロリドンを混和溶解するための良溶媒としては、N、N-ジメチルアセトアミド、ジメチルスルホキシド、ジメチルホルムアミド、N-メチルピロリドン、ジオキサンなどが好ましく用いられる。ポリスルホン系ポリマーの濃度は、10～30重量%が好ましく、15～25重量%がより好ましい。

【0030】ポリスルホン系ポリマーを不溶または膨潤させる添加剤としては、たとえば水、メタノール、エタノール、イソプロパノール、ヘキサノール、1，4-ブタンジオールなどがあるが、生産コストを考えると、水が特に好ましく使用される。ここで、水を使用した場合、ポリスルホン系ポリマーの凝固性が高いため、水の添加量は7重量%以下、特に1～5重量%が好ましい。凝固性が小さな添加剤を用いるときは添加量が多くなってもよく、適宜好適量を選択できる。

【0031】前記製膜原液を用いて製膜する方法は特に限定されず、公知の方法を用いることができる。たとえば、二重環状口金から製膜原液を吐出する際に内側に注入液を流し、乾式部を走行させた後、凝固浴へ導く方法を用いることができる。この際、乾式部の湿度が影響を与えるために、乾式部走行中に膜外表面からの水分補給によって、外表面近傍での相分離挙動を速め、孔径を拡大し、結果として透析の際の透過・拡散抵抗を減らすことも可能である。ただし、相対湿度が高すぎると外表面での原液凝固が支配的になり、かえって孔径が小さくなり、結果として分離膜の透過・拡散抵抗を増大する傾向がある。そのため、乾式部の相対湿度としては60～90%が好適である。また、注入液の組成としては、プロセス適性から、製膜原液に用いた溶媒を基本とする組成からなるものを用いることが好ましい。ここで、注入液の濃度としては、例えばジメチルアセトアミドを用いたときは、45～80重量%が好ましく、より好ましくは60～75重量%の水溶液が好適に用いられる。

【0032】また、本発明においては、材料中のポリビニルピロリドンを不溶化するが、不溶化する方法として、放射線を用いて材料中に含まれるポリビニルピロリドンを架橋処理することが好ましい。

【0033】放射線処理としては、材料を湿潤状態γ線・電子線などを照射することが好ましい。ここでいう湿潤状態とは、材料を乾燥させない状態のことを言う。その程度は特に限定されるものではないが、通常、材料が材料の重量に対して1重量%以上の水分を含んでいることが好ましい。また、材料が水溶液に浸漬された状態でも良い。

【0034】放射線の吸収線量は湿潤状態で10～50

した場合は、滅菌処理を同時に行うことも可能である。この際、吸収線量は線量測定ラベルをモジュールの表面に貼り付けるなどして測定することができる。

【0035】放射線処理された材料は、血液浄化用の分離膜として好適に用いることができる。血液浄化用に用いる場合、放射線処理は同時に滅菌効果も奏することになるが、滅菌効果が不足する場合は、放射線照射してポリビニルピロリドンを不溶化した後、蒸気滅菌などを行えば、血液浄化用材料として好適に使用可能である。

10 【0036】放射線の吸収線量が10kGy未満ではポリビニルピロリドンが不溶化されにくい。また、50kGyより照射量が多くなると支持体であるポリスルホンやケースなどの他の素材への劣化の影響が大きくなることがある。

【0037】ポリビニルピロリドンを不溶化したまま、ポリビニルピロリドンの可動性量を上げるためには、ポリビニルピロリドンを含む材料を架橋阻害剤を含む水溶液に湿潤させた状態で放射線処理を施すことにより得ることができる。

20 【0038】該架橋阻害剤としては、架橋反応を阻害するものであれば特に限定されるものではないが、血液浄化用途に用いる際は、その安全性を考慮する必要があるため、毒性の低いものが好適に用いられる。なかでも水溶性ビタミン、グリセリン、エタノール等のアルコール類、ポリフェノール、ポリエチレンイミン、ポリエチレングリコール、トレハロースなどの糖類、ピロ亜硫酸ナトリウム、炭酸水素ナトリウムなどの無機塩、酸素、二酸化炭素などが挙げられ、好適に使用される。これらの架橋阻害剤は単独で用いてもよいし、2種類以上混合して用いてもよい。

30 【0039】架橋阻害剤を含有する水溶液の濃度については、含有する架橋阻害剤により好適な範囲が異なるが、いずれの架橋阻害剤を用いる場合でも、ポリビニルピロリドンの可動性量を300以上、可溶性量を15%重量以下にする必要がある。例えば、グリセリン水溶液の場合、グリセリン濃度は0.1重量%以上、10重量%以下、エタノール水溶液の場合は0.01重量%以上、5重量%以下、ポリエチレンイミン水溶液の場合は0.01重量%以上、5重量%以下であることが好適であるが、その他の架橋阻害剤の場合は、好適な濃度範囲をそれぞれ選択することができる。

40 【0040】また、可溶性を15重量%以下にするためには架橋阻害剤の選定だけでなく、放射線を照射する前のポリビニルピロリドンの分散状態を適度に保つことが好ましく、適度にポリビニルピロリドンが接触、絡み合った状態であることが好ましいと考えられる。方法としては、可溶性が15重量%以下になるように、材料の組成、混合方法、成型方法を選択すれば良いが、例えば、成膜原液中のポリビニルピロリドン含有量を高くするこ

ニルピロリドン含有量を高くすれば架橋が進み、可動性を高く維持したままで可溶性を低くすることが出来る。例を挙げるとポリスルホンとPVPをジメチルアセトアミドに十分溶解した後にジメチルアセトアミドを蒸発、乾燥させたポリスルホン/ポリビニルピロリドン平膜においては平膜中のポリビニルピロリドン含有量が1重量%の場合は放射線照射後にすべてが溶解してしまったが、ポリビニルピロリドンの含有量が6.6重量%の場合は組成以外は同一の成膜、放射線処理条件であっても可溶性は1.5重量%以下であった。中空糸膜の場合においても一例を挙げると重量平均分子量が4.5万より大きいポリビニルピロリドン8重量%以上、ポリスルホン1.8重量%、水1重量%と残りがジメチルアセトアミドからなる成膜溶液を用いて、中空糸膜を作成し、グリセリン濃度0.1重量%～1.0重量%を含む水溶液で γ 線照射することにより得られる。また、この他の場合において、可動性が低い場合は架橋阻害材の量を多くする、可溶性が高い場合はポリビニルピロリドンの含有量を多くするなどの条件を適宜選択すれば目的となる材料を得ることが出来る。

【0041】ここでいうポリビニルピロリドンの可溶性量は次の通りにして求められる。すなわち、乾燥した材料を、N-メチル-2-ピロリドンに2.5重量%の濃度に溶解し、その溶液に水を1.7倍量添加して、素材ポリマーを析出させる。可溶性のポリビニルピロリドンは、分散したポリスルホン微粒子とともに溶液中に含まれる。溶液中のポリスルホン微粒子をHPLC（高速液体クロマトグラフィー）用の非水系フィルター（東ソー製、2.5 μ 径）でろ過して除去し、ろ液中に含まれるポリビニルピロリドンをHPLCにて定量する（装置：Waters、GPC-244、カラム：TSK gel GMPWXL2本、溶媒：水径、0.1M塩化アンモニウム、0.1Nアンモニア、pH9.5、流速：1.0ml/min、温度：23℃）。ろ液中に含まれるポリビニルピロリドンの量から材料の単位重量あたりに含まれるポリビニルピロリドンの可溶性量を求め、それを元素分析から求められる材料の単位重量あたりに含まれる全ポリビニルピロリドンの量で割った値が可溶性量（%）である。

【0042】さらに、ここでいうポリビニルピロリドンの可動性量は下記の通りにして求められる。

【0043】すなわち、高分解能MAS（Magic Angle Spinning、マジック角度回転法）溶液プローブを用いたNMR（核磁気共鳴分析法）を使用する。具体的には、蒸留水で洗浄した湿润状態の分離膜を大過剰の重水に浸漬し、重水置換する。同時にこの操作によって架橋阻害剤などの添加物も可能な限り除去する。次に重水で置換された試料（乾燥したときの試料重量は5mg）を容量40 μ lの専用セルに湿润したまま詰め、VARIAN社製UNITY IN

時間を設定する。内標としてTSP：3-トリメチルシリル7- β -D-ガラクトナトリウム-2,2,3,3-d₄の重水溶液約10 μ g添加、H₂Oピークをプレサチュレーションによって消去、MAS回転数1600～1800Hzとする）。得られたスペクトルにおいて、TSPのピーク（-0.2～0.2ppm）の積分値を100.00とした時、2.9～4.2ppmに位置するポリビニルピロリドン由来のピーク面積を求める。その付近に架橋抑制剤（例えばポリエチレンイミン）に由来するピークで妨害される場合は、1.4～2.6ppmに位置するポリビニルピロリドン由来のピーク面積を求め、種々の可動性をもつ試料の1.4～2.6ppmと2.9～4.2ppmのピーク面積から作成された検量線から2.9～4.2ppmに位置するポリビニルピロリドン由来のピークの実面積を求めることができる。本ピーク面積は材料に含まれるポリビニルピロリドンの量に対応する。そこでポリビニルピロリドンの可動性量とは、上記のようにして求められるピーク面積を元素分析から求められる材料中の全ポリビニルピロリドンの割合（%）で割ったものをいう。

【0044】なお、材料中の全ポリビニルピロリドン量は、元素分析により求めることができる。すなわち、乾燥した材料0.2～0.5mgを横型反応炉（800～950℃）で気化・酸化させ生成した一酸化窒素を化学発光法で測定する（装置は三菱化学製TN-10を使用）。定量は予め、含窒素ポリマーの標準物で作成した検量線により自動的に濃度計算できる。

【0045】以下、本発明の材料が中空糸膜であるときの血小板付着実験方法を記載する。

【0046】中空糸分離膜を30本束ね、中空糸中空部を閉塞しないようにエポキシ系ポッティング剤で両末端をガラス管モジュールケースに固定し、ミニモジュールを作成する。該ミニモジュールの直径は約7mm、長さは約10cmである。該ミニモジュールの血液入口と透析液出口をシリコンチューブで繋ぎ、血液出口から蒸留水100mlを10ml/分の流速で流し、中空糸およびモジュール内部を洗浄した後、生理食塩水を充填し、透析液入口、出口をキャップする。次に、中空糸側を0.59ml/分の流速で、2時間生理食塩水ブラッシングした後、3.2%クエン酸三ナトリウム2水和物水溶液と家兔新鮮血を1：9（容積比）で混合した血液7mlを0.59ml/分の流速で1時間灌流する。その後、生理食塩水で10mlシリンジにて洗浄し、3%グルタルアルデヒド水溶液を中空糸側、透析液側に充填し、一晚以上置き、グルタルアルデヒド固定を行う。その後、蒸留水にて、グルタルアルデヒドを洗浄し、ミニモジュールから中空糸膜を切り出して乾燥した。この中空糸膜の内表面を走査型電子顕微鏡にて観察し、1.12 $\times 10^3 \mu m^2$ の面積中の付着血小板数を数えた。付着血小板数は、少ない方が優れた分離膜である。中空糸膜の形態でない場合は血液に材料を浸漬して、付着状態を

置き、血液を入れるなどして、適宜行えばよい。

【0047】本発明における材料は、透明樹脂、コンタクトレンズ眼内レンズその他の医療用ハイドロゲル材料、血液透析膜、人工腎臓などの血液浄化用材料として好適に使用することができる。

【0048】

【実施例】実施例におけるNMR測定においては、分離膜は膜の1000倍重量の重水に12時間冷蔵浸漬した。測定は45°パルスで繰り返し時間10秒にて行った。

【0049】（実施例1）ポリスルホン（テイジンアモコ社製“ユーデル”P-3500）18部、ポリビニルピロリドン（BASF社製“コリドン”30）9部をN、N-ジメチルアセトアミド72部、水1部に加え、90℃14時間加熱溶解した。この製膜原液を外径0.3mm、内径0.2mmのオリフィス型二重円筒型口金より吐出し芯液としてジメチルアセトアミド58部、水42部からなる溶液を吐出させ、乾式長350mmを通過した後、水100%の凝固浴に導き中空糸膜を得た。得られた中空糸の径は内径200μm、膜厚40μmであった。得られた中空糸膜をグリセリン1重量%を含む水溶液中でγ線照射した。γ線吸収線量は28kGyであった。この中空糸膜中のポリビニルピロリドンの可動性量、可溶性量、血小板付着数を表1に示した。

【0050】（実施例2）実施例1と同様にして得られた中空糸膜を、グリセリン0.5重量%を含む水溶液中でγ線照射した。γ線吸収線量は29kGyであった。この中空糸膜中のポリビニルピロリドンの可動性量、可溶性量、血小板付着数を表1に示した。

【0051】（実施例3）実施例1と同様にして得られた中空糸膜を、グリセリン0.1重量%を含む水溶液中でγ線照射した。γ線吸収線量は29kGyであった。この中空糸膜中のポリビニルピロリドンの可動性量、可溶性量、血小板付着数を表1に示した。

【0052】（実施例4）実施例1と同様にして得られた中空糸膜を、ポリエチレンイミン（和光純薬、分子量7万）1重量%を含む水溶液中でγ線照射した。γ線吸

* 収線量は29kGyであった。この中空糸膜中のポリビニルピロリドンの可動性量、可溶性量、血小板付着数を表1に示した。なお、可動性量については、2.9～4.2ppmに位置するポリビニルピロリドン由来のピークはポリエチレンイミンに由来するピークで妨害されたため、1.4～2.6ppmに位置するポリビニルピロリドン由来のピーク面積を求め、1.4～2.6ppmと2.9～4.2ppmのピーク面積から作成された検量線から2.9～4.2ppmに位置するポリビニルピロリドン由来のピークの面積を求めた。

【0053】（比較例1）実施例1と同様にして得られた中空糸膜を、水中でγ線照射した。γ線吸収線量は29kGyであった。この中空糸膜中のポリビニルピロリドンの可動性量、可溶性量、血小板付着数を表1に示した。

【0054】（比較例2）実施例1と同様にして得られた中空糸膜を、グリセリン80重量%を含む水溶液で湿潤させた状態でγ線照射した。γ線吸収線量は29kGyであった。この中空糸膜中のポリビニルピロリドンの可動性量、可溶性量、血小板付着数を表1に示した。

【0055】（比較例3）市販の旭メディカル社製“APS-150S”（ロット番号008L8V-S、γ線滅菌済みのもの）から中空糸を取り出した。この中空糸膜中のポリビニルピロリドンの可動性量、可溶性量、血小板付着数を表1に示した。

【0056】（比較例4）市販の川澄化学製“PS-UW”（ロット番号082675、高圧蒸気滅菌済みのもの）から中空糸を取り出した。この中空糸膜中のポリビニルピロリドンの可動性量、可溶性量、血小板付着数を表1に示した。

【0057】（比較例5）実施例1と同様にして、グリセリン0.05重量%を含む水溶液中でγ線照射した。γ線吸収線量は27kGyであった。この中空糸膜中のポリビニルピロリドンの可動性量、可溶性量、血小板付着数を表1に示した。

【0058】

【表1】

	可動性量	可溶性量(重量%)	血小板付着数
実施例1	911	10.3	18
実施例2	1159	8.3	17
実施例3	716	7.7	20
実施例4	1940	12.2	9
比較例1	147	3.5	47
比較例2	1220	73.3	5.7
比較例3	1036	19.5	0
比較例4	1263	46.3	0
比較例5	280	5.1	29

【0059】表1から実施例の分離膜は、いずれも血小

ニルピロリドンの可動性量が小さい比較例（比較例1、

ロリドンの可溶性量が大きすぎる比較例（比較例2、3、4）は、血小板付着数は少ないが、可溶性のポリビニルピロリドンの溶出が懸念される。

【0060】

* 【発明の効果】本発明の材料およびその製造方法は、血液浄化器などの用途に用いられ、特に抗血小板附着性に優れた材料を提供でき、極めて有用なものである。

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